Research Plan of the Wayne State University Center for Urban African American Health

The thematic focus for the WSU CPHHD grant application is uncovering new ways to redress health disparities of African Americans by improving diet and other lifestyle factors including physical activity, and reducing obesity and other risk factors for cardiovascular disease, cancer, and other chronic diseases. We chose African Americans as the sole study population for all of our Projects because they are the largest minority group in the United States, and because they suffer excessively from a wide range of obesity and lifestyle-related health conditions. Importantly, the proposed research Projects will explore the primary as well as interactive effects of social environmental exposures (individual, household and community-level), psychological and genetic factors to physiological (e.g., 24-hour BP burden and oxidative stress), biochemical, and anthropometric mediators of our study outcomes. Our research efforts seek to understand the mechanisms mediating known disparate health conditions, their precursors, and to elucidate therapeutic approaches that might reduce the disproportionate burden of disease in African Americans.

The Metropolitan Detroit area comprises a unique demographic setting for this Center. In the 2000 census, Detroit had the **third** largest population of African-Americans among all cities in the nation (Year 2000 Census Data), and ranked **first** in the percentage (81.6%) of African Americans among all cities over 100,000 population. In addition, the index of dissimilarity between whites and African-Americans, a measure of segregation, shows the Detroit metropolitan area to be the most segregated in the nation (Glaeser EL and Vigdor JL, 2001).

A. Specific Aims

1) To elucidate the environmental, psychosocial, biological, and genetic factors, as well as their interactions, and the mediators of their effects, on physiological responses
Hypothesis: *Psychosocial factors will independently impact as well as interact with biological and genetic factors to explain a significant proportion of the variation in physiological responses to interventions undertaken*

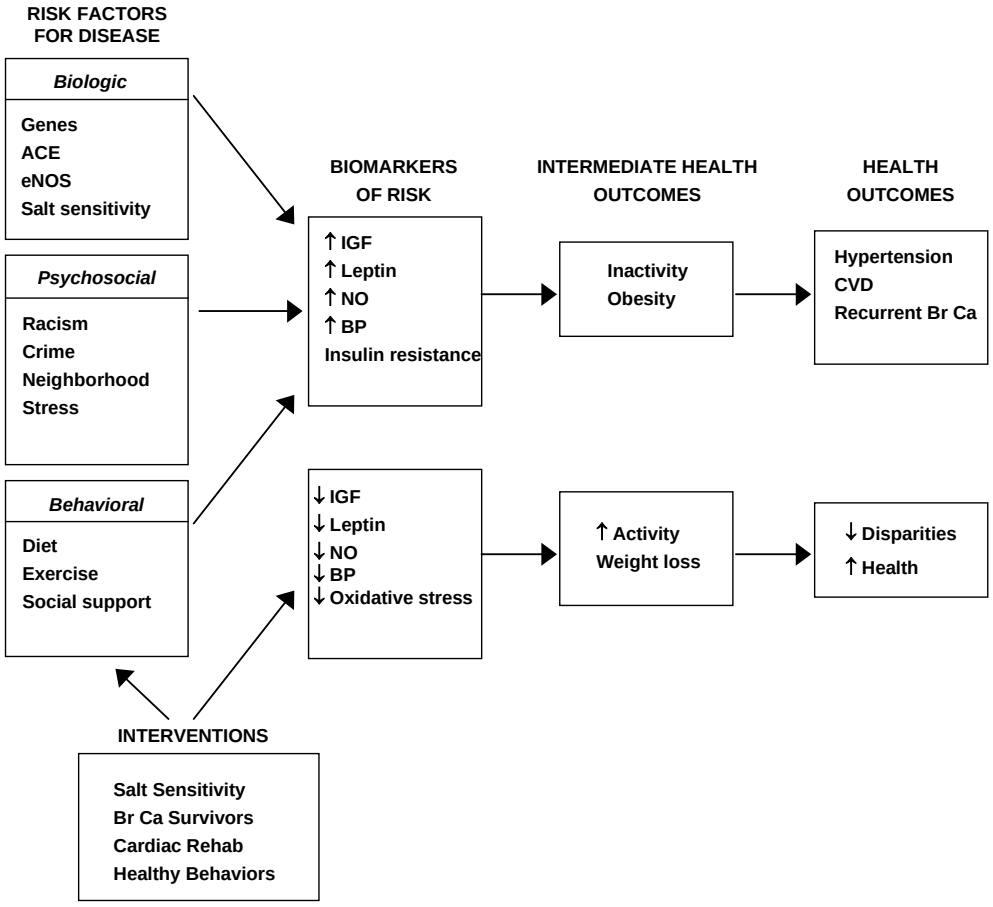
2) To better understand the relationship of environmental exposures, socioeconomic status and psychosocial factors to biological, and genetic characteristics of free-living African Americans
Hypothesis: *Environmental and psychosocial factors will correlate differentially with biological and genetic factors, and better understanding of these relationships will facilitate development of interventions to favorably affect modifiable factors*

3) To understand the contribution of environmental, social support, and individual characteristics that predict the success or failure of multi-faceted interventions that promote adoption of healthy lifestyles
Hypothesis: Environmental and individual attributes will impact the adoption of multi-faceted lifestyle interventions

4) To determine whether patients with advanced cardiovascular disease are more likely to adopt healthy lifestyles, and improve both physiological measures and disease-specific process of care measures, when counseling is provided to dyads versus counseling only of the affected patient
Hypothesis: Counseling of dyads will prove more effective than solely counseling individual patients affected with advanced cardiovascular disease

5) To develop a multi-disciplinary research infrastructure to effectively integrate established investigators as well as to identify and mentor junior investigators by providing shared research support consisting of essential research services and equipment, cognitive expertise, and a sense of common purpose for the pursuit of multi-level research into racial/ethnic health disparities

Figure 1. Specific Aims for the WSU Center for Urban African American Health



A.1. Linkage of Center to Karmanos Cancer Institute:

The Comprehensive Karmanos Cancer Institute (KCI) has an integral role in the operations of the proposed Center. The nutritional assessments, dietary counseling and intervention services, selected laboratory services, and investigator participation and expertise are provided to the Center from Karmanos Cancer Institute faculty. Karmanos Cancer Institute faculties have leadership and advisory committee positions in this Project. For example, Dr. Richard Severson, a key KCI faculty member, is Co-PI of the WSU Center and chairs the committee in charge of the pilot study program. Dr. Zora Djuric, another KCI faculty member, is not only a Project Investigator, but also brings invaluable laboratory measurement expertise and nutritional assessment and intervention skills to the Project. Dieticians from KCI will participate in the Recruitment and Clinical Measures Core to perform the actual nutritional assessments and dietary interventions. Other KCI faculty will have advisory board and committee appointments in the Center. Dr. Judith Abrams, the head of the Biostatistics and Research Database Core, is another key KCI faculty who brings a wealth of clinical trial and general statistical expertise to the Center. Dr. Jill Barnholz-Sloan, another KCI faculty, is a Co-Investigator in Project #1(Flack PI) where she brings critical genetic epidemiology expertise to the Center. Karmanos Cancer Institute personnel have key roles in the Center's operations, governance, and scientific direction. The success of the Center in regards to testing proposed hypotheses and carrying out assessments and interventions is inextricably linked to KCI expertise and key personnel. KCI faculty will participate in the educational, scientific, and administrative conferences of the Center. Furthermore, they will link the Center to other investigators and provide a venue for the dissemination of the scientific activities of the Center into KCI and vice versa.

B. Background and Significance

Cross-sectional data indicate that approximately 22% of US adults participate in **no** leisure time physical activity [LTPA] with women being less active than men (27% versus 17%, respectively) (Crespo C, Keteyian

S, Heath G, et al., 1996). Forty percent of African-American women are physically inactive, and African-American women have the greatest age-related decrease in the cross-sectional prevalence of physical activity. Data from the Coronary Artery Risk Development in Young Adults [CARDIA] Study showed that African-American women had 2.7 kg/m^2 higher age-adjusted mean BMI, higher total energy intake, lower levels of physical activity, and lower physical fitness than White women (Burke GL, Savage PJ, Manolio TA, et al., 1992). The prevalence of obesity in the USA doubled from 13% to 27% in the 39-year period between 1960 and 1999 (Must, Spadano, Coakley et al,1999; NCHS, 2000). The prevalence of obesity and overweight (BMI 25-29.9 kg/m^2) is higher in African Americans than whites at every educational level in NHANES III with the highest rates in the lowest SES strata (Winkleby MA, Kraimer HC, Ahn DK, et al., 1998).

Obesity-related chronic conditions such as stroke, coronary heart disease, heart failure (Gillum RF, 1996), and kidney disease all are excessively prevalent amongst African Americans. Furthermore, the major risk factors for cardiovascular-renal diseases - hypertension (Gillum RF, 1996), diabetes (Nzerue CM, Demissochew H, and Tucker JK, 2002; Clark, Ferdinand, Flack, et al., 2001), and cigarette smoking (McGrady GA, Ahluwalia JS, and Pederson LL, 1998; Resnicow K, Futterman R, Weston RE, et al., 1996) - are disproportionately prevalent in African Americans compared to the Whites. Obesity is not only an important antecedent of diabetes mellitus (Field AE, Coakley EH, Must A, et al., 2001) and hypertension (Gillum RF, 1996), but is also an independent risk factor for heart failure (He J, Ogden LG, Bazzano LA, et al., 2001; Kenchaiah S, Evans JC, Levy D, et al., 2002), ESRD, coronary heart disease (Field AE, Coakley EH, Must A, et al., 2001), stroke mortality (Perry IJ and Beevers DG, 1992; Walker SP, Rimm EB, Ascherio A, et al., 1996), colon cancer (Ford ES, 1999), and total mortality (Stevens J, Plankey MW, Williamson DF, et al., 1998, Baik I, Ascherio A, Rimm EB, et al., 2000, Calle EE, Thun MJ, Petrelli JM, et al., 1999, Jousilahti P, Tuomilehto J, Vartiainen E, et al., 1996).

Cancer is the second leading cause of death among Americans and is responsible for one of every four deaths in the United States (US). African Americans are more likely to develop *and* die from cancer than any other racial or ethnic group. From 1992 to 1998, the average annual death rate per 100,000 people for all cancers combined was 218.2 for African Americans, 164.5 for whites, and 102.6 for Hispanics, (CDC, 2002). African Americans have the highest death rate from colorectal cancer of any racial or ethnic group in the US, and the death rates for prostate cancer were more than twice as high for African Americans than for whites. The risk of breast cancer in obese post-menopausal women is 50% higher, and the risk for colon cancer in men by 40% (Harvard Center for Cancer Prevention, 1996; Levi F, 1999) relative to sex-matched non-obese persons. African American women with breast cancer have more aggressive disease and lower survival than do White women (Campbell JB, 2002). In addition the relative risks of gallbladder and endometrial cancer are five times higher for obese individuals compared with “healthy” weight individuals (Levi F, 1999). Moreover, a direct association between measures of body weight and renal cell adenocarcinoma (Lew EA and Garfinkel L, 1979; Tavani A and La Vecchia C, 1997) has been documented.

C. Settings and Facilities

Wayne State University has made a strong commitment to this Project by undertaking substantial salary cost-sharing, providing 2 - 4 graduate research assistants per year to the Center, and identifying administrative space to house administrative and key scientific personnel. Included in this area will be space for research and administrative meetings and conferences. If needed, additional clinical space for the performance of clinical visits will be identified and leased by Wayne Sate University. See the letter of support from Dr. Dan Walz, Associate Dean for Research and Graduate Programs at Wayne State University. Administrative support, at no cost, from the University has already been provided to the Principal Investigator and Business Manager to aid in the preparation this Center grant. This considerable institutional support will greatly facilitate the conduct of proposed Center activities and demonstrates the importance that Wayne State University places on this Center.

The Recruitment and Clinical Measures Core housed in the Department of Medicine CRC, the site of the majority of the Project clinical study visits, and the Karmanos Cancer Institute’s dieticians who are a shared resource for the Projects and perform the dietary assessments and counseling for three of the four Projects. The majority of participant recruitment for Projects will occur in this Core as well.

The Wayne State University Applied Genomics Technology Center is a state-of-the-art facility encompassing a wide range of genomic and post-genomic technologies and the expertise and track record to work with research scientists across the campus and the State of Michigan. There is the instrumentation and skill-set within the Center to perform not just high-throughput genomics, but the bioinformatics tools to investigate the results. The Center has been designated as the *State of Michigan Life Sciences Corridor's Genomics Facility*. The Center is *CERTIFIED* by on-site inspections at the State (CLIA-88) and soon will be certified at the Federal level (ASHG, CAP).

D. Proposed Use of Human Volunteers

Human subjects will be used for all of the Projects. All of the Projects are clinical trials involving either administration of sodium and/or placebo (Project 1, Flack PI), dietary change interventions (Projects 1,2, and 4), measurement of body composition (all Projects), as well as performance of measurements on urine, blood, and genetic samples. Questionnaire data will be obtained from all participants in all Projects. All participants will provide informed consent prior to any participation in the study-related activities. Study personnel and investigators will receive University-mandated training regarding the ethical conduct of clinical research. Participant safety will be safeguarded in multiple ways. First, there are limits to the level of dietary change that will be undertaken in any patient. Study eligibility criteria and participant monitoring protocols during the course of the trials also ensure patient safety. Finally, the Data Safety and Monitoring Board will view un-blinded data for each Project in regards to adverse events, morbidity, mortality, recruitment strategies, and participant drop-out rates. A Medical Director as well as a physician assistant are budgeted for the Center. They will respond to medical emergencies, perform physical exams, review abnormal laboratory data, respond to alert values, and will work closely with the study coordinators in the performance of these tasks.

E. Organization and Administration

These Cores represent the shared research infrastructure of the Center.

1. Administrative Core, PI: John M. Flack, M.D., M.P.H., Co-PI: Drs. Severson and Nies, Business Manager: Amanda Dudley, B.S., Administrative Assistant, Erikka Cullum
   This Core will be responsible for coordinating all research, administrative, fiscal and educational activities of the Center as well as for coordinating all external communications, advisory board and committee meetings. This Core will coordinate all committee and advisory board meetings, will collect and disseminate their reports, and maintaining a master file of these reports and meeting minutes. The Administrative Core Business Manager, Ms. Amanda Dudley, who is accountable to the Internal Steering committee through the Center PI, Dr. Flack.

   The administrative structure of the center comprises both an Internal and External Advisory committee. These committees will provide scientific and administrative oversight and direction to the center, funded research projects and pilot studies. The center will also establish a Data Safety and Monitoring Board, which will provide oversight to data collection, study auditing and assure protection of human subjects. The center will have one central Community Advisory Board (CAB) that will be made up of community leaders and residents of the Detroit community. The CAB will actively advise the center Investigators and core leaders in matters regarding recruitment strategies study interventions and conduct. The center will also develop an Executive Management Team, which will oversee the day to day operational activities of the center. All these components function cooperatively to form a systematic structure for the conduct of research. A more detailed description of the administrative structure of the center and its components are described in the Administrative Core.

2. Psychosocial and Community Measures Core, PI: Janet Hankin, Ph.D. [Sociology]
   This Core will provide expertise to all Projects in regards to the hypotheses and standard instruments for measurement of individual, household, and community-level variables that facilitate or hinder the adoption of healthy lifestyle behaviors and also influence physiological variables such as blood pressure response to dietary sodium. Another Core activity will be the provision of methodological consultation and cultural validation of all individual-level psychosocial measures, and relevant community-level measures, across Center Projects and pilot studies.

3. Recruitment and Clinical Measures Core, Director: Dorothy Nelson, Ph.D. Co-Director: Peter Lichtenberg, Ph.D. [Institute of Gerontology]
This Core will coordinate recruiting efforts for all Projects and pilot studies in conjunction with the investigators and will house key staff assigned to the four Projects and pilot studies. Also, this Core will be responsible for making nutritional assessments. Interviewer training for all Projects and pilot studies will be undertaken by this Core. Many study personnel for the Projects have been placed in this Core to facilitate staffing efficiencies, cross-training, and to provide a ready made infrastructure for cost-efficient execution of pilot studies. The location of this Core, its equipment and personnel will be in the Department of Medicine's CRC. The Karmanos Cancer Institute's Nutrition Core, equipment, and personnel will be integral components of this Core.

4. Biostatistics and Research Database Core, Director: Judith Abrams, Ph.D. Co-Director's: Amy Pienta, Ph.D. and David Womble, Ph.D.
This multi-disciplinary Core has primary responsibility for the design and development of research databases and for ensuring that all Projects are well-planned and are using appropriate experimental designs as well as for ensuring that planned statistical analyses are suitable to the experimental design and study endpoints. This Core will also oversee forms/survey instrument development for data acquisition and will be responsible for devising data handling algorithms, quality control procedures, and preparation of interim reports (e.g., recruiting updates, adverse events) for study investigators as well as for the data safety and monitoring committee. An important task assigned to this Core will be to provide assistance to investigators in the pilot study program on feasibility, design, analysis, interpretation, and data presentation issues related to their studies.

5. Genomics Core, Director, Susan Land, Ph.D.
The Genomics Core will provide the expertise, instrumentation, and bioinformatics so the Project investigators can effectively carry out molecular genomics research in a cost efficient and efficacious manner. This includes technical advice, DNA extraction, genotyping, and data analysis. Supplemental technologies including expression analysis, DNA sequencing, and chromosomal analysis are also available. The ultimate goal of the Core is to provide the expertise and high throughput genetic analysis necessary to study the connection between environment, SES, genes, obesity, lifestyle factors and health.

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